46, respectively, are added, to resolve the objection to claims 6, 7 and 9, at page 3 of the July 2, 2002 Office Action, as depending from succeeding claims. Withdrawal of that objection is therefore respectfully requested.

Rejections under 35 U.S.C. 102(b)

Claims 6, 7, 9 (now 44, 45 and 46, respectively), 37 and 40 stand rejected under 35 U.S.C. 102(b) as being anticipated by Sayers et al., Soc. Neurosci. Abst. 1998, 24: abstract 125.2. It is asserted that Sayers et al. anticipates the rejected claims because that reference teaches the use of 1 mg/kg/day clenbuterol in treating spinal cord injury. Applicants respectfully request reconsideration and withdrawal of this rejection based on the following discussion.

Sayers et al. actually teaches the use of 1 mg/kg/day clenbuterol to aid in "behavioral recovery following spinal cord injury". However, Sayers et al. does not teach the use of β_2 adrenergic agonists, including clenbuterol, for treating a spinal cord injury itself. That reference, and all other cited references, only teach the use of β_2 adrenergic agonists for improving the effects (e.g., behavioral recovery) of a spinal cord injury. In contrast, the instant specification teaches that β_2 adrenergic agonists are useful for treating the spinal cord injury itself, thus increasing locomotor function and neuromuscular strength, as claimed. Thus, Sayers et al. only describes the use of clenbuterol for improving the toe spreading behavioral response, and not the claimed response of locomotor function and neuromuscular strength. Additionally, Sayers et al. only describes treatment for an injury at the T8 level of the spine, not at the claimed "lower thoracic spine" as claimed. As discussed in the Reply dated March 25, 2002, "lower thoracic spine" is the T10-T12 level, not the T8 level.

Since Sayers et al. does not describe (a) the claimed administration of clenbuterol

to a mammal with a lower thoracic spine injury, or (b) the use of clenbuterol for increasing locomotor function and neuromuscular strength, applicants assert that Sayers et al. does not anticipate the rejected claims. Withdrawal of the rejections under 35 U.S.C. 102(b) is therefore respectfully requested.

Rejections under 35 U.S.C. 103(a)

Claims 1, 4, 42 and 43 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Sayers et al. It is asserted that the rejected claims are obvious because "the effect of clenbuterol in the instant method of treatment is known and the optimization of result effect parameters ... is obvious as being within the skill of the artisan, absent evidence to the contrary." Applicants respectfully request reconsideration and withdrawal of this rejection based on the following discussion.

As previously discussed, the instant invention first discloses that β_2 adrenergic agonists are effective in treating spinal cord contusion injury or motor neuron degeneration. Sayers et al. only discloses that clenbuterol is effective in treating a particular behavioral effect of a spinal cord contusion injury. However, Sayers et al. does not teach that clenbuterol or any other β_2 adrenergic agonist can treat the contusion injury itself. Thus, the instant specification teaches a previously unappreciated effect of β_2 adrenergic agonists in treating spinal cord contusion injuries and motor neuron degeneration. As such, the methods disclosed in Sayers et al. or any other cited prior art would not be understood to be effective at the claimed dose because, at the time of filing, the skilled artisan believed that β_2 adrenergic agonists were only effective on behavioral effects of a spinal cord contusion injury, and not on the injury itself. Thus, the instant specification establishes that β_2 adrenergic agonists could be used at a much lower dosage than previously appreciated because the specification establishes that the

effects of β_2 adrenergic agonists on spinal cord contusion injuries are much more significant than previously appreciated.

Based on the above discussion, the applicants assert that the instant specification establishes that β_2 adrenergic agonists, including clenbuterol, have clear and convincing unexpected results on spinal cord injury and motor neuron degeneration that are of statistical and practical significance, because β_2 adrenergic agonists were previously only thought to affect behavioral effects of spinal cord injury. Establishing that β_2 adrenergic agonists affect the actual injury and not just the behavioral effects would lead the skilled artisan to understand that β_2 adrenergic agonists are effective at lower doses than appreciated.

Claims 1, 4, 6, 7 (now 44, 45 and 46, respectively), 9, 37, 40, 42 and 43 also stand rejected under 35 U.S.C. 103(a) as being unpatentable over Etlinger et al., WO99/09966. It is asserted that the teaching in Etlinger et al. that scoliosis can be treated with 0.5 to 1000 μg/kg/day makes the instant claims obvious. Applicants respectfully request reconsideration and withdrawal of these rejections based on the following discussion.

Etlinger et al. only teaches that β_2 adrenergic agonists are effective in treating the effects of scoliosis, that is an asymmetrical muscle weakness on one side of the spine. As such, although scoliosis may be caused by a spinal cord contusion injury or motor neuron degeneration, Etlinger et al. says nothing about treating a spinal cord contusion injury or motor neuron degeneration, per se. Therefore, Etlinger et al. does not make the instant claims obvious because that reference only discusses the use of β_2 adrenergic agonists in treating one possible behavioral effect of a possible result (scoliosis) of a spinal cord contusion injury or motor neuron degeneration, and not the injury or degeneration itself. Rather, the effective treatment of the injury or degeneration is first

taught in the instant specification.

Based on the above, Etlinger et al. would not lead the skilled artisan to understand that β_2 adrenergic agonists are effective in treating a spinal cord contusion injury or motor neuron degeneration because that reference does not teach that β_2 adrenergic agonists are effective in treating the injury or degeneration itself. For these reasons, applicants respectfully request withdrawal of the rejections under 35 U.S.C. 103(a) as being obvious over Etlinger et al.

Conclusion

In light of the claim amendments and the above discussion, applicants respectfully request withdrawal of all current rejections and the search and examination of the claims encompassing the nonelected species. If there are any minor issues preventing this, applicants urge that the examiner contact the undersigned attorney.

Respectfully submitted,

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December 30, 2002

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1. A method of rehabilitation following spinal cord contusion injury or motor neuron degeneration, the method comprising administering to a mammalian patient with spinal cord contusion injury or motor neuron degeneration causing reduction of locomotor function and neuromuscular strength, a therapeutically effective amount of at least one β_2 adrenergic agonist to increase locomotor function and neuromuscular strength in the patient, wherein the effective amount of the β_2 adrenergic agonist is from about 0.5 to about 100 μg per kg of body weight.

4. The method of claim 1, wherein the β_2 adrenergic agonist comprises clenbuterol or a salt thereof.

37. A method of rehabilitation following spinal cord contusion injury to the lower thoracic spine, the method comprising administering to a mammalian patient with spinal cord contusion injury in the lower thoracic spine causing reduction of locomotor function and neuromuscular strength, a therapeutically effective amount of at least one β_2 adrenergic agonist to increase locomotor function and neuromuscular strength in the patient

40. The method of claim 37 wherein the β_2 adrenergic agonist comprises clenbuterol or a salt thereof.

42. The method of claim 1, wherein the effective amount of the β_2 adrenergic agonist is from about 10 to about 100 μg per kg of body weight.

43. The method of claim 1, wherein the effective amount of the β_2 adrenergic agonist is about 40 μg per kg of body weight.

44. (New) The method of claim 37 wherein the effective amount of the β_2

adrenergic agonist is from about 0.5 to about 1000 μg per kg of body weight.

45. (New) The method of claim 40 wherein the effective amount of clenbuterol is from about 0.5 to about 1000 μg per kg of body weight.

46. (New) The method of claim 40, wherein the effective amount of clenbuterol is greater than about 0.25 mg/day per kg body weight.